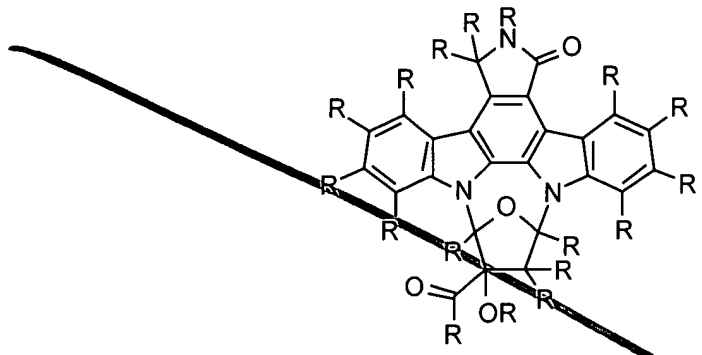


wherein R is selected from the group consisting of a C_{3-10} branched or unbranched alkyl, including Me optionally partially or fully halogenated; an hydroxy; a C_{1-3} alkyloxy, including CO_2Me; a carboxy; an amino; an alkylamino; a hydrogen; a halogen; Bn; DMB ; PMB; and mixtures of any of these, and wherein X is O and/or S.

REMARKS

Claims 1 to 20 were pending in this application prior to entry of the above amendments. Claims 1 and 17 have been amended. Allowance of the amended claims is requested in view of these remarks.

This invention relates to the synthesis of glycosylated indolocarbazoles of biomedical use. These remarks address issues raised by the Examiner in the order presented in the Office Action, and are numbered accordingly.

2. Priority. The undersigned is puzzled by the priority questions raised in this portion of the Action and respectfully traverses the assessment. The parentage of this application is clearly set out in the files of the international PCT application, the national phase entry application, and the C.I.P. replacing it, and correctly reported in the filing receipt. The claimed invention of the above-referenced divisional is clearly set out in all three, particularly as ring expansion and contraction are reversible using Applicants' processes. Both PCT/IB96/00987 and U.S. Pat. Ap. Ser. No. 08/817,230

contained a much broader definition of R groups than what was particularly pointed out and distinctly claimed in U.S. Pat. Ap. Ser. No. 09/206,082 (which issued as U.S. 6,037,468), which certainly encompass narrower species, and so the earlier parents' claims clearly disclose the invention claimed herein, which is also narrower and tracks the language of Ser. No. 09/206,082, only cut back to advance prosecution and avoid breadth arguments with the Examiner. Both John L. Wood and Brian M. Stoltz are common inventors. And claim 3 was retained throughout. Applicants' priority claims are fully supported in the file wrappers of the parent applications.

3/4. Specification Objections. The specification was objected to for the abstract's length. A substitute abstract is included herein, which shortens the originally presented abstract to include only subject matter claimed in this divisional application.

Though Applicants incorporated by reference publications and patents that should assist persons skilled in the art to practice the claimed invention, there was no representation in this extended courtesy to the public that incorporated material is "essential" for the practice of the invention. What is "essential" is what is determined by the inventors describing the chemistry of the invention to those skilled in the art, and the burden of proof is on the Examiner to show how Applicants neglected to provide "essential" information required for practicing the processes of the invention to obtain desired products. Moreover, spectral data and the like physical characterizations of reactants and products published elsewhere could hardly be considered "essential" in a description of how to make a glycosylated indolocarbazole, and this requirement was not made in the parent case which presented an identical specification to the Patent Office. Certainly Applicants can add verbiage to this application if required to do so to advance this case to allowance, but this is unnecessary as the Detailed Description adequately describes the processes and products, and the examples illustrate several embodiments.

5/6. 35 U.S.C. 112 Rejections. Claims 6-8, 10-12, and 18 to 19 were rejected under 35 U.S.C. 112 as being indefinite. The undersigned thanks the Examiner very much for pointing out that X in claims 1 and 17 was inadvertently omitted. Claims 1 and 17 were amended to particularly point out that X is S and/or O; support for the amendment can be found in the specification on page 9 under the illustrated structures. Applicants believe the generic definitions of R in claims 1 and 17 provide antecedent bases for the specific R groups particularly pointed out in claims 6 to 8, 12, and 19, but have further amended independent claims 1 and 17 to avoid an argument on this point and advance the application to allowance. Support for the specific R groups may be found in the specification on pages 14, 15, 17, 21, and 22 under the structures.

The rejection of claims 11 and 19 in this regard is respectfully traversed. K252a is a specific furanosylated indolocarbazole of the invention, and so is encompassed by the generic structure set out in claims 1 and 17.

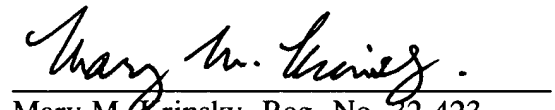
35 U.S.C. 102 Rejections. Claims 6 to 10 and 10 to 12 were rejected under the statute as anticipated by Wood, *et al.*, *Tetrahedron Lett. 37*: 3929-3930 (1996) and Wood, *et al., J. Amer. Chem. Soc. 117*: 10413-10414 (1996). The rejection is respectfully traversed. The introductory paragraphs of the *Tetrahedron* paper simply summarize the *J.A.C.S.* paper. All of the synthesis and product characterizations set out in the *J.A.C.S.* paper were included in the original U.S. provisional application Ser. No. 60/002,164, filed 08/11/95, prior to publication of the work described in the paper, and from which this application descends. Therefore, the papers are not prior art to this application.

The claims in this application are group I claims directed to furanosylated indolocarbazoles using the restriction scheme set out in parent case U.S. Ser. No. 08/817,230 in a November 26, 1997 Office Action. That group was invented by John Wood and Brian Stoltz. Therefore,

Must be deleted as they were on U.S. Pat. No. 6,037,468. Though these scientists collaborated with Dr. Wood on various aspects of the glycosylated indolocarbazole research, they are not inventors of the claimed furanosylated indolocarbazole processes. As evidenced by Yale invention disclosure #756 filed in the university's Office of Cooperative Research (a copy of which is attached hereto as Exhibit A), John L. Wood and Brian M. Stoltz are inventors of the claimed processes of the invention. This response is therefore also a petition under 37 C.F.R. section 1.48(b)(1), and the fee set forth in 1.48(b)(2) and 1.17(I) is authorized in the transmittal letter accompanying this amendment.

Applicant submits that these amendments and remarks put this application in condition for allowance, and request early and favorable consideration. If the undersigned can advance the prosecution of this application in any way, the Examiner is invited to call at the number listed below.

Respectfully submitted,



Mary M. Krinsky, Reg. No. 32,423
Attorney for Applicants
79 Trumbull Street
New Haven, CT 06511-3708
203-773-9544

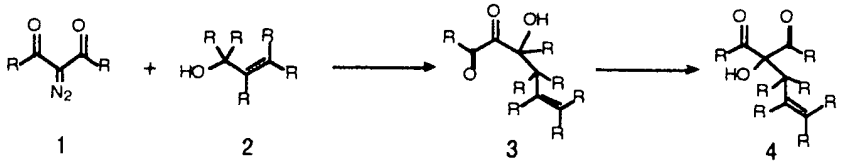
Marked Up Version of Amendments Required by 37 C.F.R. Section 1.121

Specification:

Abstract

[Tertiary alcohols containing the structural features illustrated in **3** or **4** below (Scheme I) are prepared by reacting at least one diazo carbonyl compound, *e.g.*, **1** in Scheme I) and at least one allylic alcohol (*e.g.*, **2** in Scheme I) in a coupling reaction run under conditions that produce carbene or carbenoid intermediates from the diazo-containing substrate such as transition metal catalysis or either thermal or photochemical decomposition. In some preferred embodiments, $Rh_2(OAc)_4$ is employed to catalyze the coupling reaction.

Scheme I

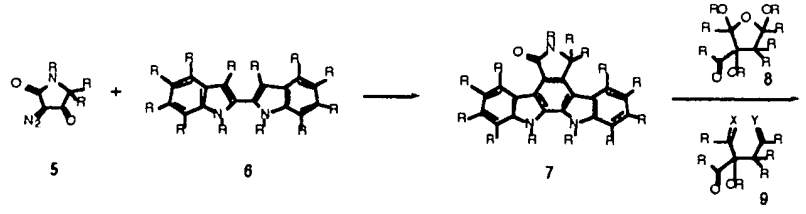


1 2 3 4

Wherein R represents a substituent comprised of any number and combination of the elements H, C, N, S,Si, O, Cl, Br, I, and F

Indolocarbazoles (*e.g.*, **7** below) are prepared by coupling of diazo carbonyl compounds (*e.g.*, **5**) and biindoles (*e.g.*, **6**).] Indolocarbazoles are furanosylated (*e.g.*, **7**) with acetals (*e.g.*, **8**) or their open chain congeners (*e.g.*, **9**) under conditions known to promote acetal exchange or formation, such as protic or Lewis acids. Furanosylated indolocarbazoles (*e.g.*, **10**) are also prepared via ring contraction of pyranosylated indolocarbazoles (*e.g.*, **11**) under conditions know to effect oxidation and benzylic acid type rearrangements, and pyranosylated indolocarbazoles (*e.g.*, **11**) are prepared via ring expansion of the furanosylated congeners (*e.g.*, **10**).

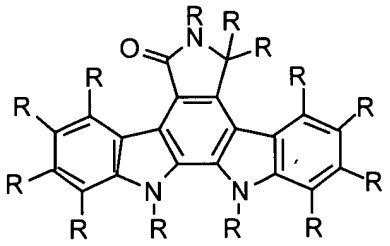
[Scheme II]



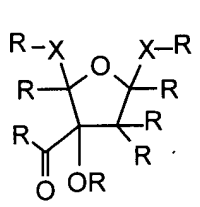
5 6 7 8 9

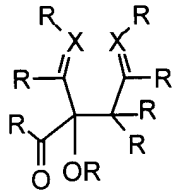
Claims:

1 (Amended). A process for the preparation of furanosylated indolocarbazoles by reacting an indolocarbazole of the formula



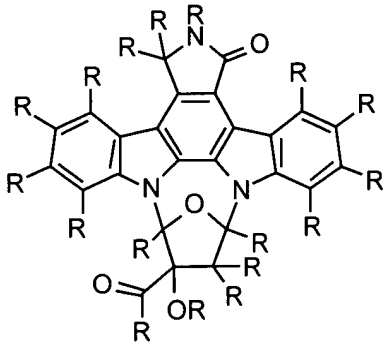
with an acetal selected from the group consisting of the formulae





and mixtures thereof,

to produce a glycosylated product of the formula



wherein R is selected from the group consisting of

a) a C_{3-10} branched or unbranched alkyl, optionally partially or fully halogenated, hydroxy, C_{1-3} alkyloxy, carboxy, amino, alkylamino, including Me, CH_2OH, and CO_2 Me;

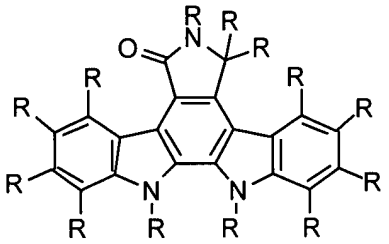
b) an aryl optionally substituted with one to five groups consisting of halo, hydroxy, C_{1-3} alkyloxy, including Bn, DMB, and PMB;

c) a hydrogen;

d) a halogen; and

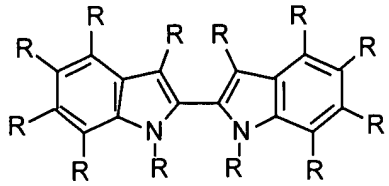
e) mixtures of any of these and
wherein X is S and/or O.

17 (Amended). A process for the preparation of furanosylated indolocarbazoles by first preparing an indolocarbazole of the formula

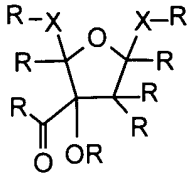


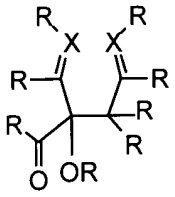
by reacting a diazo compound of the formula

with a biindole of the formula

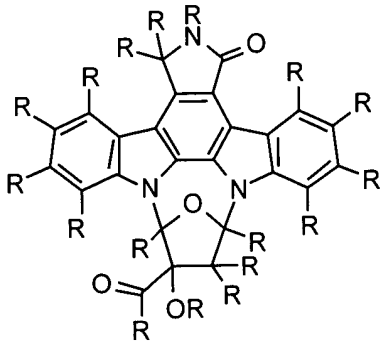


in the presence of a transition metal catalyst in a solvent capable of solvating the reactants, and then reacting the indolocarbazole with an acetal selected from the group consisting of the formulae





and mixtures thereof, in the presence of a Bronsted acid or a Lewis acid to produce a glycosylated product of the formula

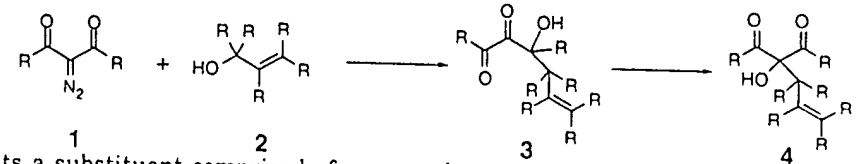


wherein R is selected from the group consisting of a $C_{3\text{-}10}$ branched or unbranched alkyl, including Me, optionally partially or fully halogenated; an hydroxy; a $C_{1\text{-}3}$ alkyloxy, including CO_2Me; a carboxy; an amino; an alkylamino; a hydrogen; a halogen; Bn; DMB; PMB; and mixtures of any of these, and wherein X is O and/or S.

We Claim:

1. A process for the asymmetric construction of tertiary alcohols containing the structural features illustrated in either **3** or **4** (Scheme I). The process utilizes at least one diazo carbonyl compound (e.g., **1** Scheme I) and at least one allylic alcohol (e.g., **2**, Scheme I) in a coupling reaction that is run under conditions known to produce carbene or carbenoid intermediates from the diazo containing substrate.

Scheme I



1 2 3 4

(R represents a substituent comprised of any number and combination of the elements H, C, N, S, O, Cl, Br, I, F)

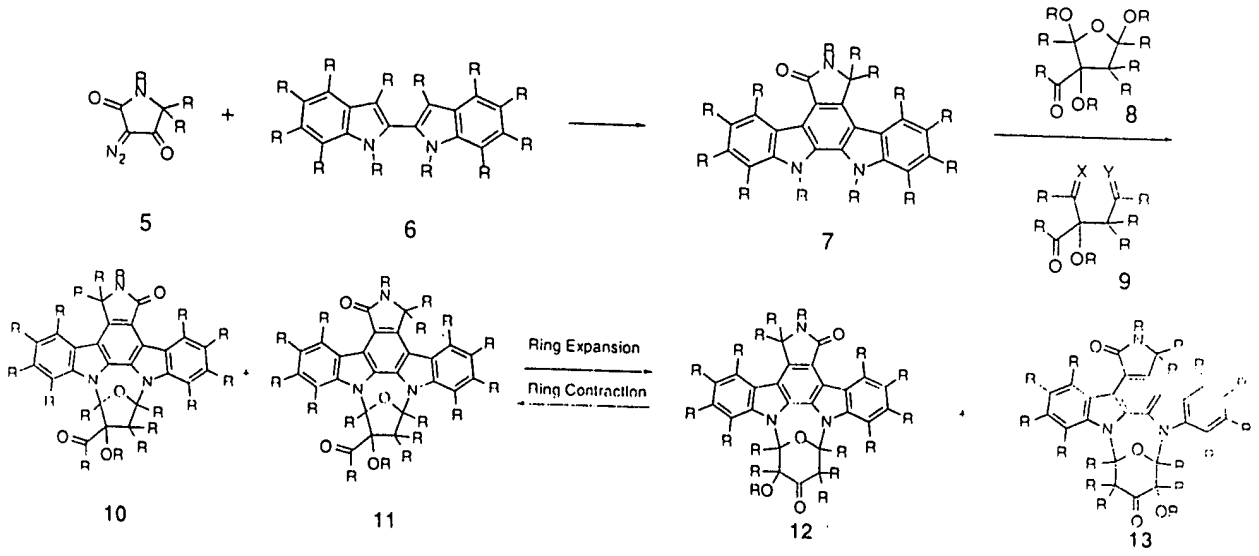
2. A process for the construction of indolocarbazoles (e.g., **7**) from the coupling of diazo carbonyl compounds (e.g. **5**) and biindoles (e.g., **6**).

3. A process for the furanosylation of indolocarbazoles (e.g., **7**) with acetals (e.g., **8**) or their open chain congeners (e.g., **9**) that produces the glycosylated products (e.g., **10**) in stereocontrolled fashion.

4. A process for the construction of furanosylated indolocarbazoles (e.g., **10**) via the ring contraction of pyranosylated indolocarbazoles (e.g., **11**).

5. A process for the construction of pyranosylated indolocarbazoles (e.g., **11**) via ring expansion of the furanosylated congeners (e.g., **10**).

Scheme II



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